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Original Research

# Comparison of opioid and opioid-free anesthesia in bariatric surgery

Multimodal anesthesia in bariatric surgery

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#### Abstract

Aim: Opioids are widely used in anesthesia. Postoperative nausea and vomiting (PONV) is known to have side effects such as tremors and urinary retention and so on. Several studies have been conducted in recent years indicating that multimodal analgesia reduces opioid consumption. There are very few studies comparing opioid-free anesthesia with Laparoscopic Sleeve Gastrectomy (LSG). The aim of this study is to evaluate the effects of opioid-free anesthesia on pain scores and healing process in patients with LSG surgery.

Material and Method: This study was conducted on 64 cases between the ages of 18-65 prospectively in the general surgical operating room of Pamukkale University Hospital. Patients were randomly selected and grouped according to anesthesia method at the beginning of the surgery. Remifentanil as an opioid was administered for analgesia in Group I. Iv paracetamol, ibuprofen, ketamine and magnesium sulfate were administered in Group II. NRS was used as a pain score. Patients included in the study were followed from the beginning of the operation to the end of the postoperative 24 hours. The obtained data were analyzed using the SPSS 25 software.

Results: The body mass index (BMI) of the patients included in the study was 40 and above. In the study, women in both groups were in the majority ( $\geq$ 75%). In both groups, cesarean section was in the majority of patients in the history of a previous surgery. Patients in Group I were significantly higher when hypotension was examined. There was no significant difference in SpO<sub>2</sub><94%, obstructive respiration, nausea, vomiting, chills, tramadol use, antiemetic need and mean TOF values in postoperative recovery unit. There was no significant difference in NRS score between groups at postoperative 1, 6, 12 and 24 hours. There were partially more complications in postoperative Group I.

Discussion: There was no significant difference between non-opioid anesthesia and opioid anesthesia, but the non-opioid anesthesia protocol can be safely used in LSG.

## Keywords

Opioid-Free Anesthesia, Bariatric Surgery, NRS Score, Laparoscopic Sleeve Gastrectomy

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Corresponding Author ORCID ID: https://orcid.org/0000-0002-5621-7407 This study was approved by the Non-Interventional Clinical Research Ethics Committee of Pamukkale University (Date: 2019-12-11, No: 60116787-020/88341)

## Introduction

Bariatric surgical procedures have made great progress over time. While open surgery was initially used in bariatric surgery, advances in surgical methods and the more comfortable strategy of laparoscopic treatments for patients reduced recovery time and postoperative discomfort [1]. However, wound site discomfort persists after laparoscopic operations. The amount of opioid use and opioid-related side effects influence the duration of hospital stay. Obstructive sleep apnea (OSAS), which is frequently associated with weight, complicates the safe administration of analgesic [2,3]. A combination of analgesic agents that can target various areas of the pain region is optimal for postoperative pain control [4]. Multimodal analgesia is the combination of two or more analgesic drugs that work through distinct processes in different areas of the central nervous system, resulting in synergistic analgesia when compared to central opioids alone [5]. Multimodal analgesia lowers individual analgesic doses and adverse effects, encouraging better pain control. It also enhances analgesia efficacy and allows for a better functional state to be achieved. Multimodal analgesia is well accepted and reduces opioid consumption in orthopedic, abdominal, cardiac, and otolaryngological surgical studies [6]. However, few studies compare the effects of non-opioid use with Laparoscopic Sleeve gastrectomy (LSG). The aim of this study is to evaluate the effect of opioid-free anesthesia on pain scores and the recovery process in patients undergoing LSG surgery.

# **Material and Methods**

The research was carried out on 64 patients between the ages of 18-65, in the ASA I-III group, who applied to Pamukkale University Medical Faculty Hospital General Surgery Department for bariatric surgery. The research was carried out between 01-12-2019 and 01-05-2020 in Pamukkale University Hospital operating room. This study was a prospective, randomized (double-blind) study. Cases for the research were randomly selected (envelope technique) from patients undergoing laparoscopic sleeve gastrectomy (LSG) and divided into two groups. The patients were evaluated preoperatively and verbal and written consent was obtained by providing information about the anesthesia and analgesia method. Inclusion criteria were as follows: ASA I-II-III group patients aged between 18-65 who will undergo bariatric surgery in general surgery operating rooms, patients with a body mass index (BMI)  $\ge$  35 kg / m<sup>2</sup>, and patients whose surgery performed under general anesthesia (from incision to closure) is not expected to exceed 2 hours. Numeric Ratio Scale (NRS) was explained to the patients participating in the study the night before the operation. The pain levels of the cases in both groups were determined by the service nurse at 0 and 30 minutes and 1, 6, 12 and 24 hours after the operation. Balanced electrolyte solution solution 1000 ml was given to the patients. Local or systemic allergic complaints and hemodynamic changes were monitored periodically for 24 hours perioperatively and postoperatively. An ampule of 8 mg of dexamethasone was administered as iv push 30 minutes before admission to the operating room for postoperative nausea and vomiting prophylaxis. In the operating room, the patients were monitored and 0.05 mg/kg of

midazolam iv was administered according to ideal body weight (IBW). For induction, propofol was administered according to IBW (1.5-2 mg/kg). Lidocaine was administered as 1mg/kg IV push according to adjusted body weight (ABW). As a muscle relaxant, rocuronium iv push was administered according to IBW (0.6 mg/kg). Sevoflurane was titrated to a MAC value of 1 and a BIS monitoring value of 40-60. Rocuronium was administered in boluses with a TOF value of 0.5 and below. During the operation, iv balanced electrolyte solution was administered at a rate of 15 ml/kg/h according to IBW and this rate was reduced to 8 ml/kg/h until the end of the surgery. When MAP decreased more than 25% of normal, 250 ml bolus IV balanced electrolyte solution was administered. If the decline continued, intravenous administration of 5 mg of ephedrine was planned. The patients were divided into two groups. In Group I (Opioid (+) Anesthesia), an initial dose of 1mcg/kg was administered for 30 to 60 seconds according to IBW 0.5-1 mcg/ kg/min by continuous IV infusion in induction of remifentanil as an opioid for analgesia. A continuous IV infusion of remifentanil 0.25 mcg/kg/min (range 0.05 -2 mcg/kg/min) was administered for maintenance. Group II (Opioid (-) Anesthesia) patients received an IV infusion of 1 g of paracetamol and an infusion of 400 mg of ibuprofen IV for analgesia 30 minutes before the incision. Before the incision in the perioperative period, 0.2 mg/ kg IV bolus ketamine was administered as an IV bolus of 0.5 mg/kg according to IBW (ideal body weight) between 30-45 minutes of surgery. A 30 mg/kg bolus of magnesium sulfate was administered followed by a 10 mg/kg/h perioperative infusion. At the end of the operation, intravenous sugammadex at a dose of 2-4 mg/kg was used to antagonize the muscle relaxant effect. Pain scores, consciousness levels, and opioidrelated side effects (nausea, vomiting, constipation, inability to urinate, difficulty concentrating, lethargy, confusion, fatigue, itching, dry mouth, headache) of patients were followed up and recorded at postoperative 1<sup>st</sup> and 30<sup>th</sup> minutes and 1<sup>st</sup>, 6<sup>th</sup>, 12<sup>th</sup> and 24<sup>th</sup> hours. Postoperative analgesia was applied depending on the NRS score. Analgesia was not administered to patients with an NRS score of less than 5. Paracetamol 1000 mg IV infusion was administered to patients with NRS scores between 5 and 8. Tramadol iv 100 mg infusion (2 hours) was administered to patients with NRS >8. In the postoperative LSG protocol, the patient was mobilized, if no dizziness or nausea was observed, between postoperative 6-8 hours.

## Statistical analysis

Sample size calculation was performed to determine the number of patients to be included in the pre-study groups. As a result of the power analysis, the study was performed on 64 patients. The data were analyzed with the SPSS package program. Continuous variables were presented as mean ± standard deviation and categorical variables were presented as numbers and percentages. Since the parametric test assumptions were met, one-way analysis of variance (Independent Samples T-test) was used to compare differences between independent groups. Differences between categorical variables were analyzed by Chi-square analysis.

# Ethical Approval

Ethical approval for the study was obtained from Pamukkale University Non-Interventional Clinical Research Ethics

## Committee (11.12.2019/ 60116787-020/88341).

# Results

When the distribution of the clinical data of the patients between the groups was examined, age, height, weight, body mass index (BMI), anesthesia and surgery durations in the groups were found to be within the same range (p>0.05). There was no statistically significant difference between the gender distribution and the ASA class values of groups (p>0.05). When the SpO2 values of the patients were examined, no significant difference was present between the groups. When the BIS score was examined, no statistically significant difference was found between the beginning of the perioperative period, 5<sup>th</sup> min, 10<sup>th</sup> min, 45<sup>th</sup> min, 60<sup>th</sup> min, 75<sup>th</sup> min, 90<sup>th</sup> min, 105<sup>th</sup> min and 120<sup>th</sup> min (p>0,05). There was no significant difference between the groups in terms of operation time. (Group 1: 99.97min /Group2: 97.19min p: 0.203). A statistically significant difference was found in terms of BIS scores between the groups (Group I>Group II) at the  $15^{th}$  and  $30^{th}$  minutes. When TOF values were examined, no statistically significant difference was found

Table 1. Change in SpO<sub>2</sub>, BIS and TOF values inpatients.

Variable		Group I (n=32)	Group II (n=32)	P#
SpO <sub>2</sub>	Perioperative start	98,09±97,38	97,38±2,09	0,263
	5 <sup>th</sup> min	98,28±1,67	97,69±2,19	0,227
	10 <sup>th</sup> min	97,72±1,67	96,75±2,10	0,065
	15 <sup>th</sup> min	97,66±1,43	96,69±1,94	0,056
	30 <sup>th</sup> min	97,91±1,35	96,81±1,28	0,074
	45 <sup>th</sup> min	97,16±3,18	96,16±2,21	0,156
	60 <sup>th</sup> min	97,41±2,34	96,44±2,15	0,09
	75 <sup>th</sup> min	97,91±2,05	97,06±1,74	0,081
	90 <sup>th</sup> min	98,06±1,67(n=31)	97,50±1,83	0,207
	105 <sup>th</sup> min	97,75±1,48(n=24)	97,29±1,55(n=24)	0,3
	120 <sup>th</sup> min	97,93±1,71(n=15)	97,60±1,84(n=10)	0,647
	Perioperative start	97,13±2,97	97,03±2,86	0,898
	5 <sup>th</sup> min	43,99±1,80	44,07±1,86	0,869
	10 <sup>th</sup> min	46,89±2,92	46,88±3,09	0,982
	15 <sup>th</sup> min	43,97±0,66	43,42±0,88	0,007
	30 <sup>th</sup> min	44,06±0,61	43,56±0,58	0,002
BIS	45 <sup>th</sup> min	43,72±1,43	43,27±0,99	0,156
	60 <sup>th</sup> min	44,51±4,06	43,40±0,97	0,134
	75 <sup>th</sup> min	63,57±6,18	62,80±4,94	0,582
	90 <sup>th</sup> min	73,36±6,04	72,82±5,76	0,716
	105 <sup>th</sup> min	75,12±7,25	76,16±8,32	0,645
	120 <sup>th</sup> min	84,68±4,20	86,57±4,49	0,295
	Perioperative start	1±0	1±0	-
	5 <sup>th</sup> min	0,50±0,01	0,46±0,01	0,0001
TOF	10 <sup>th</sup> min	0,47±0,01	0,46±0,01	0,045
	15 <sup>th</sup> min	0,43±0,01	0,43±0,01	0,726
	30 <sup>th</sup> min	0,43±0,01	0,43±0,01	0,922
	45 <sup>th</sup> min	0,42±0,01	0,41±0,01	0,156
	60 <sup>th</sup> min	0,42±0,01	0,42±0,01	0,09
	75 <sup>th</sup> min	0,43±0,09	0,41±0,01	0,236
	90 <sup>th</sup> min	0,54±0,19	0,53±0,18	0,985
	105 <sup>th</sup> min	0,61±0,22	0,69±0,21	0,249
	120 <sup>th</sup> min	0,84±0,05	0,86±0,05	0,382

**Table 2.** Change in the perioperative bradycardia, tachycardia, hypotension and hypertension values of the patients.

Variable		Group I (n=32)	Group II (n=32)	р		
Bradycardia	Yes	5 (15,6%)	2 (6,3%)	0,213		
	No	27 (84,4%)	30 (93,8%)			
Talahan	Yes	19 (59,4%)	17 (53,1%)	0,401		
Tachycardia	No	13 (40,6%)	15 (46,9%)			
ll materia	Yes	13 (40,6%)	4 (12,5%)	0,011		
Hypotension	No	19 (59,4%)	28 (87,5%)			
Huportoncion	Yes	14 (43,8%)	18 (56,3%)	0,227		
Hypertension	No	18 (56,3%)	14 (43,8%)			
<sup>†</sup> Fisher exact chi-square test						

**Table 3.** Postoperative complications and anesthesia care unitevaluations of the patients.

Variable	Group I (n=32)	Group II (n=32)	Р
Nausea	14 (43,8%)	6(18,8%)	0,029†
Vomiting	6 (18,8%)	4 (12,5%)	0,366†
Constipation	0	0	-
Inability to urinate	2 (6,3%)	0	0,694†
Difficulty in concentrating	1 (3,1%)	0	0,5†
Numbness	1 (3,1%)	0	0,5†
Brain fog	0	1 (3,1%)	-
Tiredness	14 (43,8%)	17 (53,1%)	0,309†
Itching	1 (3,1%)	0	0,5†
Dry mouth	17 (53,1%)	17 (53,1%)	0,599†
Headache	2 (6,3%)	1 (3,1%)	0,45†
${\rm SpO}_{\rm 2}$ <94% (With 6 lt/min ${\rm O}_{\rm 2}$ mask)	4 (12,5%)	5 (15,6%)	0,500†
Obstructive breathing	2 (6,3%)	0	0,246†
Nausea vomiting	14 (43,8%)	6(18,8%)	0,029†
Chills	13 (40,6%)	16 (50%)	0,308†
Tramadol use	5 (15,6%)	8 (25%)	0,268†
Need for an antiemetic	6 (18,8%)	7 (21,9%)	0,500†
Mean TOF	0,89±0,02	0,89±0,03	0,999″
SBP (mmHg)	117,31±16,83	108,16±15,38	0,027"
DBP (mmHg)	71,0±9,70	67,22±7,70	0,089"
Highest HR	97,16±11,08	92,16±11,12	0,078"
Lowest HR	68,94±8,70	68,56±8,18	0,860"
NRS 1 <sup>st</sup> hour	7,88±0,33	7,48±0,34	0,054"
NRS 6 <sup>th</sup> hour	8,00±0,62	7,91±0,59	0,538"
NRS 12 <sup>th</sup> hour	6,34±0,83	6,03±0,70	0,107"

between the beginning of the perioperative period, 5<sup>th</sup> min, 10<sup>th</sup> min, 45<sup>th</sup> min, 60<sup>th</sup> min, 75<sup>th</sup> min, 90<sup>th</sup> min, 105<sup>th</sup> min and 120<sup>th</sup> min (p>0,05). A statistically significant difference was found in terms of TOF score between the groups (Group I>Group II) at the 5<sup>th</sup> and 10<sup>th</sup> minutes (Table 1). When the perioperative monitoring value of the patients was examined, there was no statistically significant difference between the groups in terms of bradycardia, tachycardia and hypertension. Hypotension was observed in 13 patients in Group I and in more patients than in Group I and II (Table 2). When the postoperative anesthesia care unit data of the patients were examined, there was no statistically significant difference between SpO<sub>2</sub><94% (with 6 It/min O<sub>2</sub> mask), obstructive respiration, chills, tramadol

use, need of an antiemetic, DBP, highest HR and lowest HR values. Nausea-vomiting was observed in 14 patients in Group I and in 6 patients in Group II, and a statistically significant difference was found. Systolic blood pressure values were higher in Group I, and a statistically significant difference was found between the groups. When the postoperative complications of the patients were examined, there was no statistically significant difference between the groups in complaints of vomiting, constipation, inability to urinate, difficulty concentrating, drowsiness, confusion, fatigue, itching, dry mouth and headache (p>0,05). When the presence of postoperative nausea was examined, nausea-vomiting was observed in 14 patients in Group I and 6 patients in Group II, and a statistically significant difference was found (p=0,029). When the NRS score changes of the patients were examined, the NRS scores between the groups were in similar ranges and there was no statistically significant difference (p>0,05). (Table 3).

# Discussion

Obesity surgery is one of the most sustainable methods of achieving weight loss. It is considered the most effective treatment for obesity because it is effective in reducing obesity-related comorbidities and deaths and improves quality of life. Although bariatric surgery, which has been going on and spreading rapidly for ten years, is believed to reduce operative trauma compared to traditional open surgery due to minimally invasive laparoscopic surgery, the surgical stress response is still evident [7]. Opioids are powerful analgesics used to treat extreme pain; They are frequently used for perioperative or postoperative pain control. However, it has been associated with the onset of chronic illness. The widespread use of opioids in anesthesia is limited by side effects such as POBK, tremor, and urinary retention [8]. In this study, we examined the effects of perioperative and postoperative opioid use and opioid-free anesthesia on pain scores and the effect on perioperative vital functions in patients undergoing bariatric surgery. In a prospective observational cohort study conducted between October 2020 and July 2021, in a meta-analysis comparing opioid-free patients and patients taking opioids, less pain in the first 24 hours and less additional opioid use in the opioid-free patient group were found [9]. In a study conducted in patients who were given remifentanil in the opioid group and ibuprofen and tramadol in the opioid-free group, it was reported that pain scores decreased gradually in the measurements made at the 1st, 3rd, 6th, 12th, 24th and 48th hours after surgery. It has been reported that the NRS score at the  $24^{th}$  hour was 6 in patients given remifentanil, and in patients given ibuprofen and opioid-free analgesia the pain score was 5 [10]. In our study, while NRS scores were around 7 in both groups at the 1<sup>st</sup> hour, they gradually decreased until the 24<sup>th</sup> hour. No statistically significant difference was found between the two groups in the NRS scan performed at the 1st, 6th, 12th and 24th hours. When the results of a prospective study including 344 bariatric patients for three years were examined, 209 (60.8%) of the patients were opioid-free and 135 (39.2%) received standard anesthesia. There was no difference between the groups in terms of demographic data, BMI, related medical problems and type of surgery. Postoperatively, no significant

difference in opioid requirement was observed between the two groups. However, it was determined that the opioid free group received a significantly lower dose of antiemetic on the 1<sup>st</sup> and 2<sup>nd</sup> postoperative days. It was stated that the duration of hospitalization was found to be significantly shorter in the opioid-free group [11]. Although the findings of this study and our study were similar, the limitations and heterogeneity of the study group may have caused the differences. The fact that nausea and vomiting were seen in fewer patients in the opioidfree groups in both studies makes this type of anesthesia more usable. A study of 257 patients who underwent laparoscopic bariatric surgery examined the use of morphine in the first 24 hours postoperatively between opioid-using and non-opioidusing groups. In summary, the main result of this study was that the proportion of patients who did not require morphine in the first 24 hours postoperatively was 87% in the opioid-free group, which was significantly higher than in the opioid-using group[ 12]. In our study, the need for additional analgesia as a need for rescue medication was more frequent in the group taking opioids. Tramadol 100 mg IV infusion was administered when NRS score was >8, paracetamol 1000 mg IV infusion was administered when NRS score was >5. Similar results are encountered in many studies and actually explain the low postoperative pain scores in opioid-free patients. In summary, there are many publications in the literature comparing opioid and non-opioid anesthesia in bariatric surgeries. The aim of this study was to describe our experience and positive effects of opioid-free anesthesia on pain scores and the recovery process in patients undergoing bariatric surgery.

In conclusion, this study examined whether opioid-free anesthesia applications, which has recently been introduced and frequently applied in bariatric surgery, make a difference and in the end, it was determined that the greatest benefit was in relation to postoperative nausea and vomiting. In addition, it was emphasized that opioid-free anesthesia would not increase the need for additional drugs in the postoperative period.

The limitations of this study may be the small sample size, the prospective randomized controlled trial, and the study involving only two surgeons.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

## Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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# Conflict of interest

The authors declare no conflict of interest.

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